ARx TECHNICAL PAPER

MICRODEP: A FAST-ACTING, HIGHLY BIOAVAILABLE THIN FILM

Reducing adverse behavioral responses with a patient-friendly, rapid-onset delivery system

INTRODUCING ARx

ARx is a trusted, full-service partner specializing in advanced drug delivery systems that enhance control of drug release, bioavailability, and patient experience. As pioneers in polymer science and alternative dosing strategies, we push the boundaries of therapeutic potential across oral, mucosal, and transdermal applications. Collaborating with pharmaceutical companies, we create patient-friendly solutions to deliver what's possible, one product at a time.

THE CHALLENGE

While effective for rapid drug delivery, traditional intravenous (IV) administration poses significant challenges, including a higher risk of adverse behavioral responses, the need for medical supervision, and poor patient acceptance. Oral administration often results in variable absorption, first-pass metabolism, and a delayed onset of action. For conditions requiring rapid therapeutic response, current delivery methods often compromise speed, safety, and patient experience. A more efficient, patient-friendly delivery system is needed to address these limitations without compromising clinical efficacy.

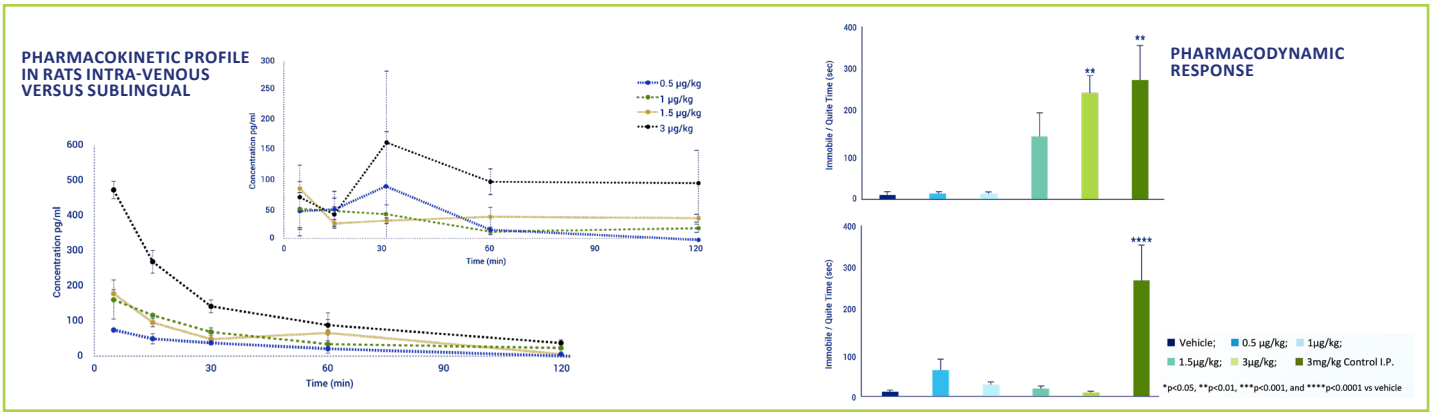
THE METHOD

ARx's MicroDEP sublingual and buccal technology leverages a proprietary micro-deposition process that enhances drug absorption through the mucosa. To evaluate MicroDEP value compared to traditional IV administration, ARx conducted comprehensive preclinical and clinical studies:

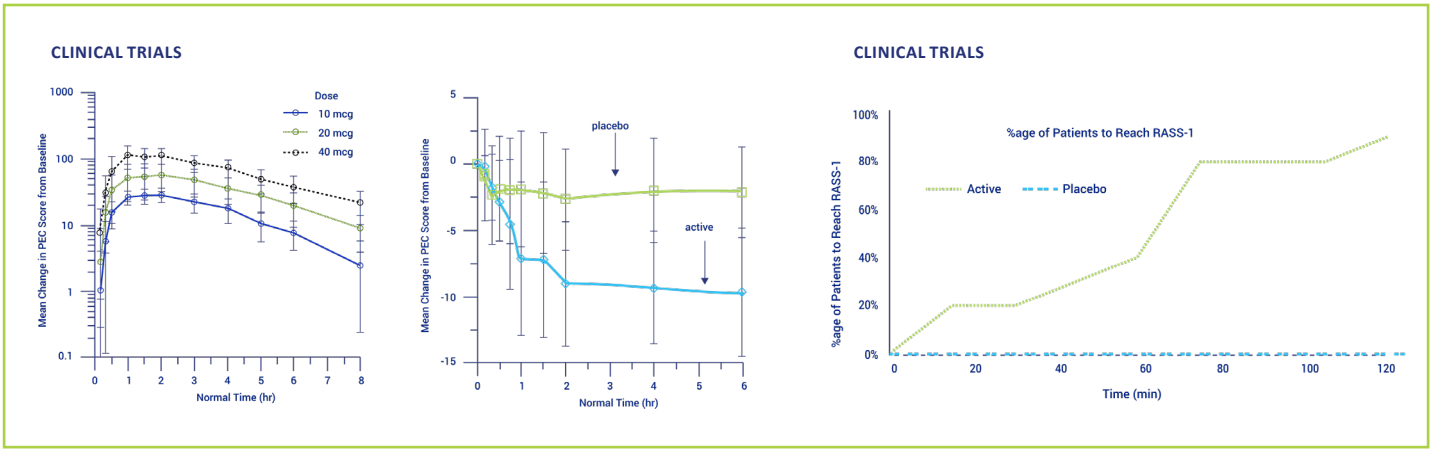
- **Pharmacokinetic Analysis:** Comparative studies in rat models evaluated plasma concentration profiles at multiple dosages (0.5, 1, 1.5, and 3 µg/kg) for both IV and sublingual administration over a 120-minute period.
- **Behavioral Assessment:** This comparative study evaluated pharmacodynamic effects across dosage forms, measuring immobility time and aggression indicators (chasing, attack, biting) to demonstrate sublingual administration was equivalent to IV for the same drug substance.
- **Clinical Efficacy Studies:** Human trials assessed therapeutic response using the Richmond Agitation-Sedation Scale (RASS-1) and Positive and Negative Syndrome Scale Excited Component (PEC) scores across multiple dosages and compared to placebo.
- **Dose-Response Evaluation:** Clinical testing of 10, 20, and 40 mcg dosages to determine optimal therapeutic range and duration of effect.

THE RESULTS

IV administration produced higher initial plasma concentrations (3 µg/kg: ~480 pg/ml) with exponential decline, while sublingual delivery showed distinct kinetics with a secondary peak at 30 minutes (3 µg/kg: ~160 pg/ml) and higher sustained levels for some doses.



IV dosing at 3 µg/kg and 1.5 µg/kg significantly increased biting behavior ($p<0.01$), likely due to rapid central nervous system penetration and resulting paradoxical excitation. In contrast, sublingual administration reduced attack behaviors across all treatment groups ($p<0.01$ to $p<0.0001$) with minimal sedation, except for the 3 mg/kg intraperitoneal control.



Sublingual treatment achieved RASS-1 target scores in 80% of human patients by 80 minutes compared to <1% for placebo, with dose-dependent PEC score improvements over placebo (40 mcg: ~100-point improvement over placebo; 20 mcg: ~60-point improvement over placebo; 10 mcg: ~30-point improvement over placebo) peaking at 2-3 hours post-administration.

THE BENEFITS

The MicroDEP sublingual system offers significant advantages over conventional IV dosing, enhancing patient comfort and safety while maintaining clinical efficacy. The system provides rapid onset of action with peak effects at 2-3 hours, addressing situations requiring prompt therapeutic response without injection administration.

This approach significantly reduces adverse behavioral effects compared to IV administration while providing more consistent, predictable clinical outcomes. The sublingual route bypasses first-pass metabolism, which may reduce systemic side effects associated with oral drugs, while maintaining therapeutic concentrations for extended periods.

Additionally, sublingual administration is noninvasive, improving patient acceptance and compliance. This makes it especially valuable for conditions where agitation or behavioral symptoms could complicate treatment.

CONTACT

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